REMARKS

Entry of the amendment is respectfully requested since it would reduce the issues on appeal and introduces no new matter. Reconsideration is also respectfully requested in light of the remarks which follow.

Claims 1-4, 6, 7, 10, 16, 17 and 20-22 are before the Examiner. Claims 6 and 20 have been cancelled. Claims 1 and 22 have been amended to include the subject matter of claims 20 and 21 except for "soluble forms of DAF, MCP and chimeric complement inhibitor proteins." Claim 22 has been further amended to address points raised in the outstanding Office Action relative to the second paragraph of 35 U.S.C. 112 rejection.

Claims 7-9, 11 and 18-19 remain withdrawn from consideration by the Examiner as directed to a non-elected invention(s).

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse.

Claim 22 has been amended to more clearly set forth the process which is old and more clearly set forth the improvement.

Withdrawal of the rejection is respectfully requested.

Claims 1-4, 6, 10, 14 and 16-17 and 20-21 are rejected under 35 U.S.C. §103(a) as being unpatentable over Terwogt (Cancer Treatment Reviews, march 1997) or O'Brien (Annals of Oncology, 1992) in view of Ko (US 5,851,528) Applicants respectfully traverse.

Claim 1 has been amended to clearly set forth the specific complement activation inhibitor present in the therapeutic composition.

Terwogt et al. teaches that paclitaxel is active clinically against advanced ovarian and breast cancer. Terwogt et al. discloses a number of problems associated with paclitaxel, e.g. poor solubility in water and with a specific formulation, a mixture of ethanol and Cremophor EL. This formulation is indicated to cause some severe hypersensitivity reactions. (The specific nature of this reaction(s) is not detailed.) Terwogt et al. review some of the most promising formulation alternatives in their article- formulations devoid of Cremophor. There is no mention of the involvement of the complement system.

Ko et al. adds little to the relevant knowledge of Terwogt et al. article in terms of the involvement of the complement system in the immediate hypersensitivity reaction caused by the

presence of specific amphiphilic carriers and the treatment of its symptoms. Ko et al. does disclose chimeric molecules composed of a first and second polypeptides, both of which inhibit complement activation. Ko et al mentions that the chimeric molecule is superior to soluble MCP or DAF in terms of this activity. See col. 2, at lines 47 plus. The chimeric proteins are taught to reduce inflammation. Conditions mentioned include those associated with ischemia-reperfusion, crash injury, burns, ARDS, autoimmune disorders, etc. Table 1, previously referred to by the Examiner, lists potential clinical targets of the protein chimeras, i.e. targets to try. [1] None is an immediate complement reaction like that claimed. While the Table does mention "Drug Allergy", drug allergies come in a variety of types, e.g. delayed and causes, and also are not an immediate hypersensitivity reaction that results from the presence of polyethoxylated or a derivatized polyethoxylated oil-carrier, a non-drug. Further, Ko et al. make no mention of the complement activation inhibitors now claimed.

O'Brien et al. reviews allergic reactions to cytotoxic drugs. Both Taxol and Cremophor are mentioned on page 609. It was reported by O'Brien et al. that in the phase I study, 2 of the first 5 patients who received Taxol as a 60-minute infusion developed anaphylactoid reactions during the first course. The other three patients developed less severe allergic symptoms during their second course. Cremophor was not proven to be the cause. The nature of the underlying mechanism is not stated by O'Brien et al. Infusion with antihistamines and pregnisole premedication is disclosed as causing the reaction to be less severe and less frequent.

It is now very clear, the combined teachings are insufficient to lead one to treat the symptoms of an immediate hypersensitivity reaction due to the presence of polyethoxylated oil or a derivatized polyethoxylated oil carrier by the inclusion of the claimed complement activation inhibitor(s) in the pharmaceutical composition containing the active ingredient. (The active ingredients are specified as taxol, paclitaxel, Doxil, althesin, cyclosporin, diazepham, didemnin E, echinomycin, propandid, steroids, teniposide, doxorubicin, daunorubicin, amphoterin B, hemoglobin, polynucleotide or a multivitamin.) None of the references unequivocally indicate polyethoxylated oil or a derivatized polyethoxylated oil carrier as the

[1] The art of pathological conditions associated with complement activation in the field of complement prior to the instant disclosed invention are described in previously submitted Table A. Applicants consulted 44 reviews, research, or textbook articles in the field. Many of these reviews, both before and after 1998 (the Ko, et al patent issued on 22 Dec 98), gave comprehensive listing of pathological conditions associated with complement activation. Each of the pathological conditions mentioned by Ko, et al are included. The first mention of immediate non-IgE hypersensitivity reactions mediated by complement was published by Applicants in Feb, 1998.

causative agent for an immediate hypersensitivity reaction. None of the references, alone or in combination, suggest the involvement of the complement system. Further, none of the references suggest the treatment of the claimed condition using a complement activation inhibitor. Further, none of the references teach or suggest the claimed complement activation inhibitors.

Added to the noted deficiencies is the state of the art at the time the application was filed. As explained in the Background section of the present application, despite extensive use of Cremophor EL in pharmaceuticals, there was no consensus in the literature regarding whether any hypersensitivity was due to an active ingredient such as paclitaxel or to the vehicle, Cremophor EL, and how the hypersensitivity reaction is mediated (see pages 2 to 7 of the specification, particularly page 3, line 31 to page 4, line 4). The state of the art at the time the application was files clearly suggest that there was not "a reasonable expectation of success." In light of these uncertainties, enumerated in the specification as filed, it can hardly be said that there was a proper prima facie case of obviousness. The rejection as stated, especially as to the claims as amended, is more akin to "obvious to try."

It is respectively submitted that a proper prima facie case has not been established for the reasons set forth above as to the invention as now claimed. Withdrawal of the rejection is respectfully requested.

In view of the foregoing amendments and remarks, the application is believed to be in condition for allowance and a notice to that effect is respectfully requested.

Should the Examiner not agree that the Application to be in allowable condition or believe that a conference would be of value in expediting the prosecution of the Application, Applicants request that the Examiner telephone undersigned Counsel to discuss the case and afford Applicants an opportunity to submit any Supplemental Amendment that might advance prosecution and place the Application in allowable condition.

Respectfully submitted,

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